European Union MDRs Impact on Device Manufacturers—A Notified Body Perspective

Medical Device Regulation 2017/745

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Mehr Sicherheit.
Mehr Wert.

Choose certainty.
Add value.

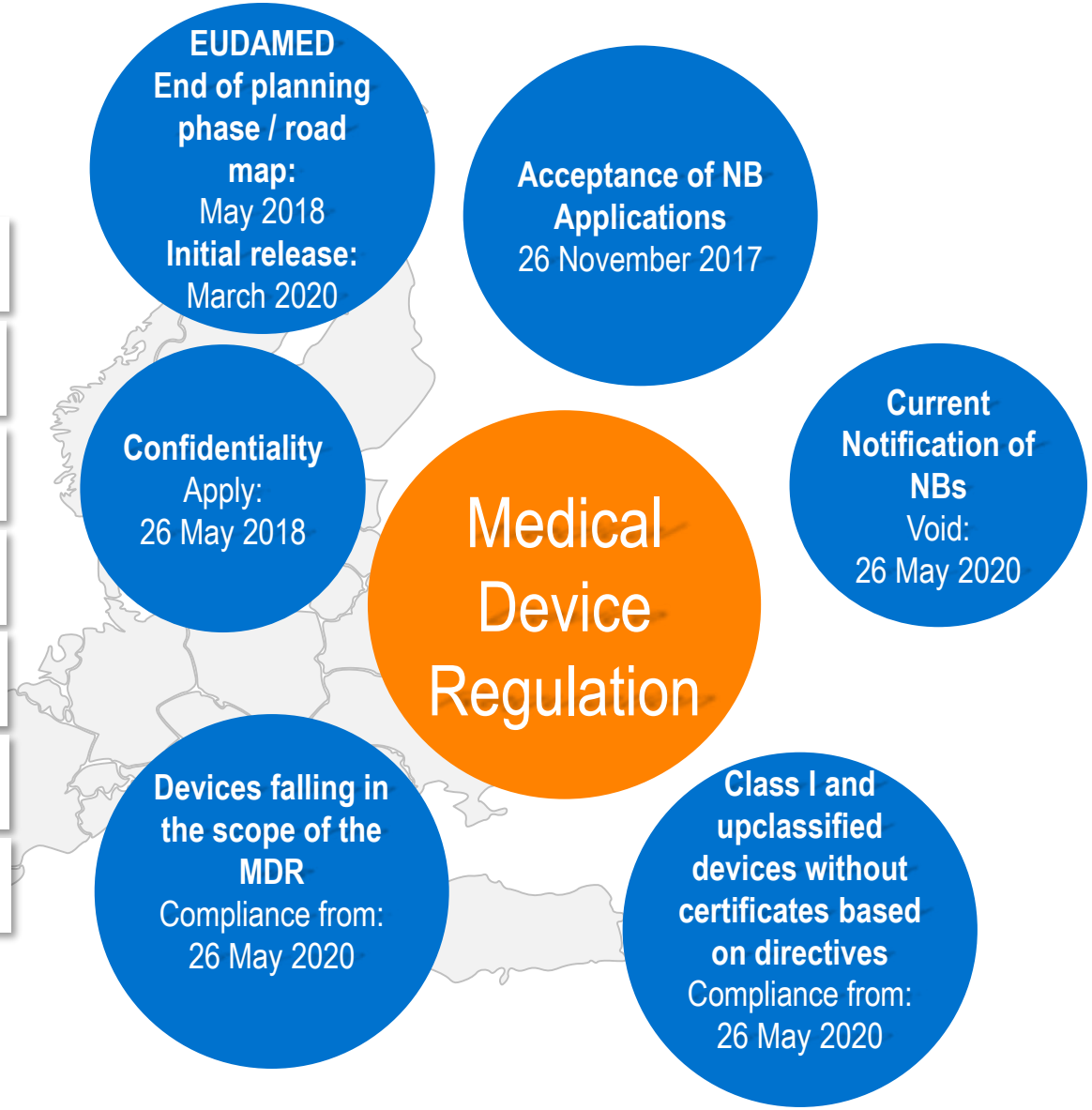
Disclaimer

This presentation is based on information available as of today and prepared to my best knowledge as subject matter expert.

This presentation presents my personal understanding of the medical device requirements in Europe and is not reflecting the view of TÜV SÜD PS.

What is happening when…

2008	Commission: consultation on medical device framework
2012	Commission: proposal for new MDR
2014 Q2	Parliament: position on MDR
2015 Q3	Council position on proposed Regulation
2015 Q4	Trilogue: Commission, Parliament, Council
2017	MDR published on May 5, 2017
2020	End of three-year transition on May 26, 2020



Additional documents to be expected

Delegating Acts

Implementing Acts

Common Specification

Harmonized Standards

Other guidance documents either as MEDDEV or similar

(e.g. CAMD)

Important timelines

Annex 4 AIMDD 90/385/EEC void 27 May 2022

Annex IV MDD 93/42/EEC void 27 May 2022

Certificates issued from 25 May 2017 shall become void at latest on 27 May 2024

From 26 May 2020 no significant changes in the design and intended purpose

From 26 May 2020 Reporting of SAE and device deficiencies per MDR

Made available or put into service until 27 May 2025

Coordinated Assessment Procedure on CI shall apply from 26 May 2027

Implementing Act / Regulation / MDCG Docs

MDCG documents

MDCG endorsed documents

Reference	Title	Publication date
MDCG 2018-1	Draft guidance on basic UDI-DI and changes to UDI-DI	March 2018
MDCG 2018-2	Future EU medical device nomenclature – Description of requirements	March 2018

Designation of notified bodies under the new Regulations on medical devices

Notified BODIES	Designation of notified bodies under the new Regulations on medical devices
	1. Best practice guidance on designation and notification of conformity assessment bodies (NBOG BPG 2017-1)
	2. Best practice guidance on the information required for conformity assessment bodies' personnel involved in conformity assessment activities (NBOG BPG 2017-2)
	3. Application form to be submitted by a conformity assessment body when applying for designation as notified body under the medical devices Regulation (MDR) (NBOG F 2017-1)
	4. Application form to be submitted by a conformity assessment body when applying for designation as notified body under the in vitro diagnostic devices Regulation (IVDR) (NBOG F 2017-2)
	5. Applied-for scope of designation and notification of a conformity assessment body – Regulation (EU) 2017/745 (MDR) (NBOG F 2017-3)
	6. Applied-for scope of designation and notification of a conformity assessment body – Regulation (EU) 2017/746 (IVDR) (NBOG F 2017-4)
	7. Preliminary assessment review template (MDR) (NBOG F 2017-5)
	8. Preliminary assessment review template (IVDR) (NBOG F 2017-6)
	9. Review of qualification for the authorisation of personnel (MDR) (NBOG F 2017-7)
	10. Review of qualification for the authorisation of personnel (IVDR) (NBOG F

Annex 1: Flowchart of activities and times

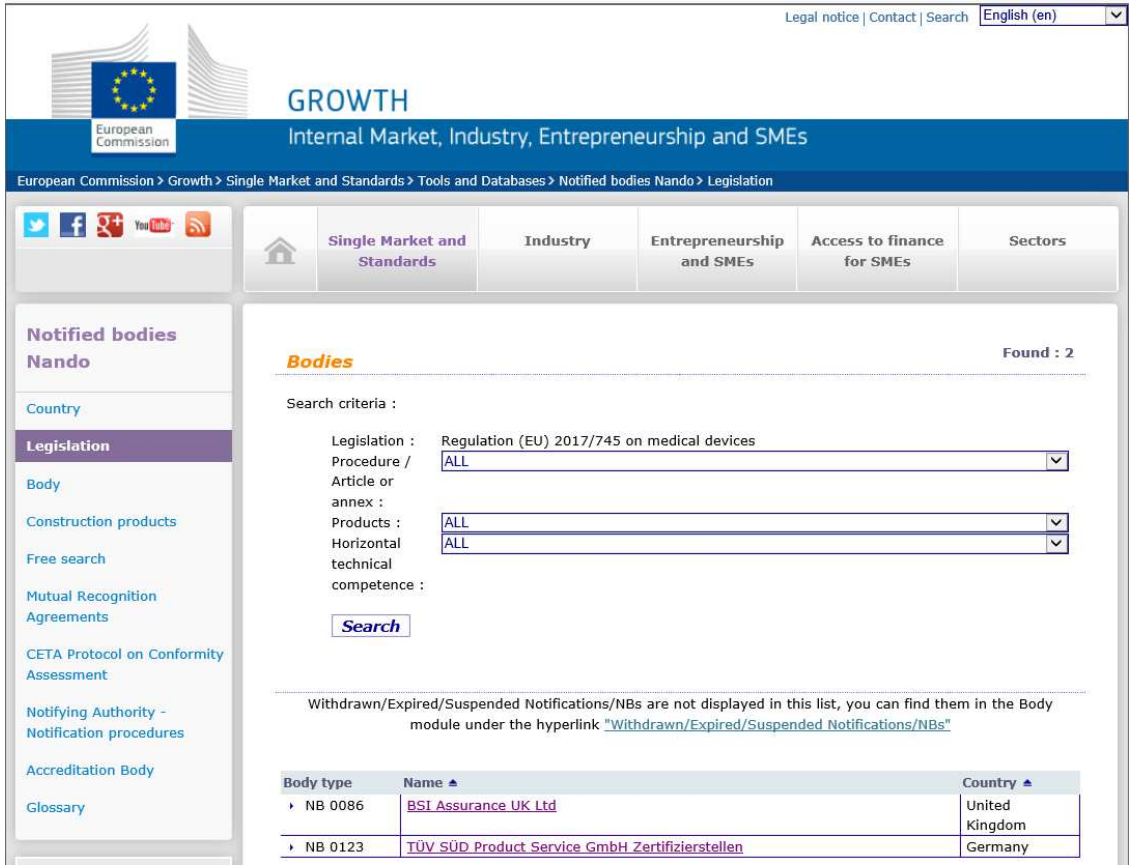
Tentative time-line	Activity	Tentative calendar for existing notified bodies (see section 2.1)
18 months in advance of repeal of relevant Directive	Application sent to the designating authority from the CAB	27 November 2017
Within 30 days of receipt of the application	Completeness check of application by the designating authority	27 December 2017
Immediately after application is considered complete	Transmission of application to SANTE/F	27 December 2017
Estimate: within 2 months after application is considered complete	Assessment of CAB's application by the designating authority and issuing of preliminary assessment report	27 February 2018
Within 14 days after receipt of preliminary assessment report	Appointment of the JAT and scheduling of the on-site assessment	13 March 2018
Within 90 days after appointment of the JAT	Formal announcement of and arrangement of practicalities for the on-site assessment Dissemination of information to JAT members Assessment of CAB application by the JAT	13 June 2018
At least 5 weeks *before* the anticipated on-site assessment	Coordination teleconference between the JAT and the designating authority	20 July 2018
On-site assessment	In accordance with the agreed assessment plan	10 September 2018
Last day of the on-site assessment	Designating authority list of non-compliances and summary of the JAT assessment to be presented at the closing meeting	14 September 2018
Timeframe defined by the designating authority	CAB's submission of the CAPA plan	September/October 2018
Within 30 days after the on-site assessment	JAT remaining diverging opinions to be sent to the designating authority	14 October 2018
Estimate: within 2 months after the on-site assessment	Designating authority's confirmation and assessment of CAB's CAPA plan. To be forwarded to the JAT	14 November 2018
Within 30 days after receipt of CAPA plan and the designating authority opinion	JAT assessment of CAPA plan and designating authority's opinion thereon. If applicable, request for modifications or clarifications	14 December 2019
Estimate: around 6 months after receipt of CAPA plan	Designating authority final assessment report after verification of implementation of CAPAs	14 May 2019
Within 21 days after receipt of the designating authority final assessment report	JAT final opinion	5 June 2019
Within 42 days after receipt of final JAT opinion	Recommendation of the MDCG on designation	17 July 2019
Undefined	Final decision on designation by the designating authority	26 July 2019
	Notification process	

26 July 2019

First Notification January 2019
Second Notification May 2019

NANDO

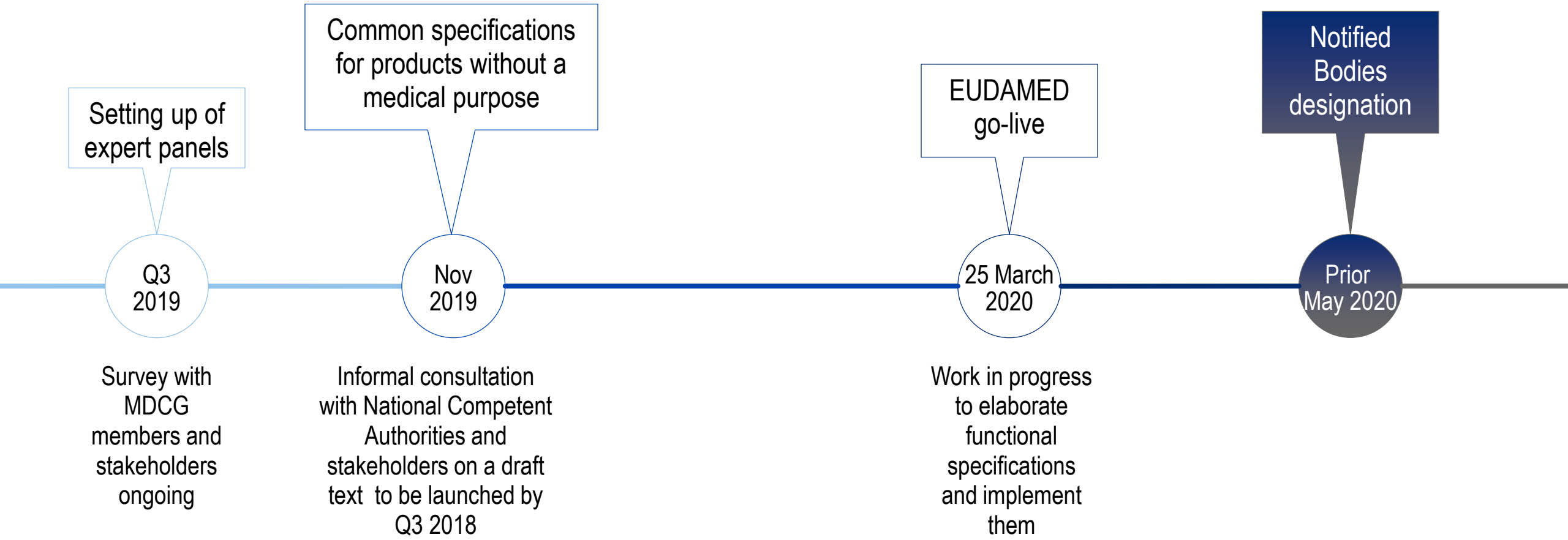
http://ec.europa.eu/growth/tools-databases/nando/index.cfm?fuseaction=directive.notifiedbody&dir_id=34



Where we are with per latest information

Source: https://ec.europa.eu/docsroom/documents/31902

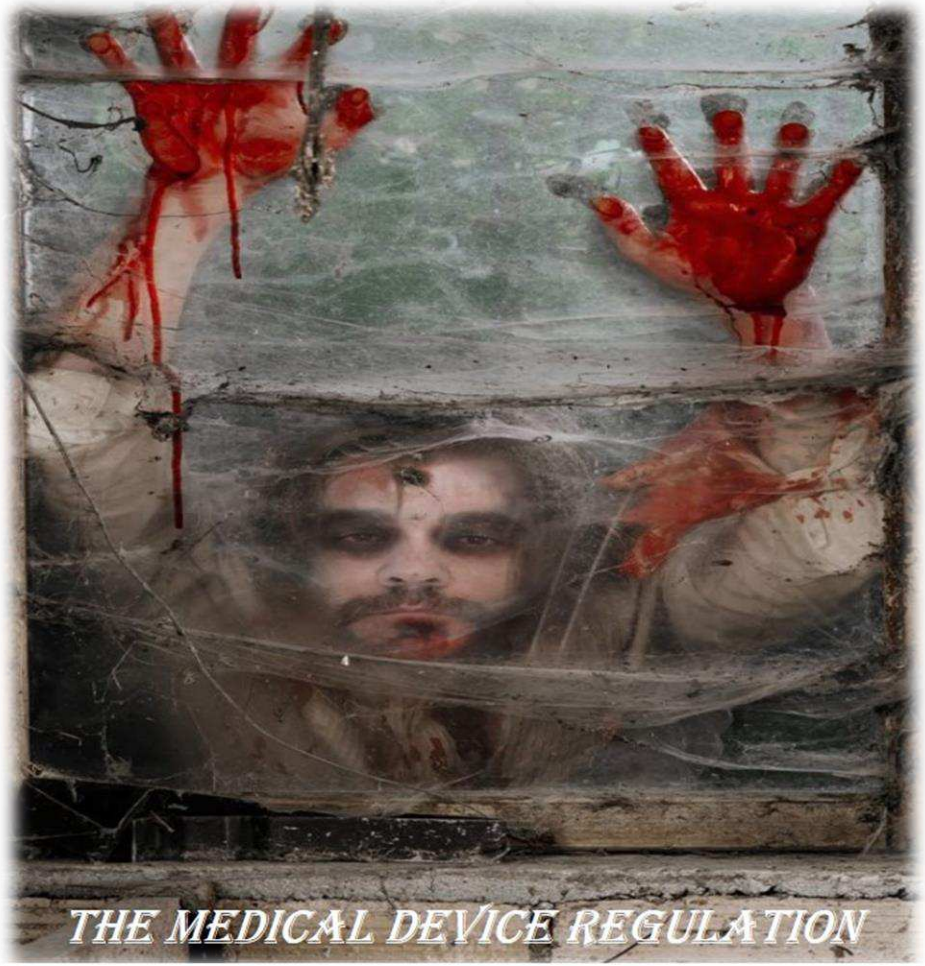
Expected timelines (expected date of final adoption/date of accomplishment)



What will industry do?

"Certificates issued by notified bodies in accordance with Directives 90/385/EEC and 93/42/EEC shall remain valid until the end of the period indicated on the certificate, which shall not exceed five years from its issuance. They shall however become void at the latest on 27 May 2024."

Moving targets and short timelines – Still approx. 380 days ☹



- ❑ Last submissions under the current legislative framework in November 2019
- ❑ First MDR application acceptance earliest in late summer 2019
- ❑ Expert panels first available in Q3 2019
- ❑ EUDAMED go-live in March 2020
- ❑ Common specifications for products without medical purpose in November 2019
- ❑ New discussion on Brexit in October 2019
- ❑ Second Corrigendum in Summer 2019

The obligations of Medical Device Manufacturers

01 Classification of the Device

02 Choice of the Conformity Assessment Procedure (check Notified Body involvement)

03 Installation and maintenance of a Quality Management System

04 Issuing new Declaration of Conformity and CE marking

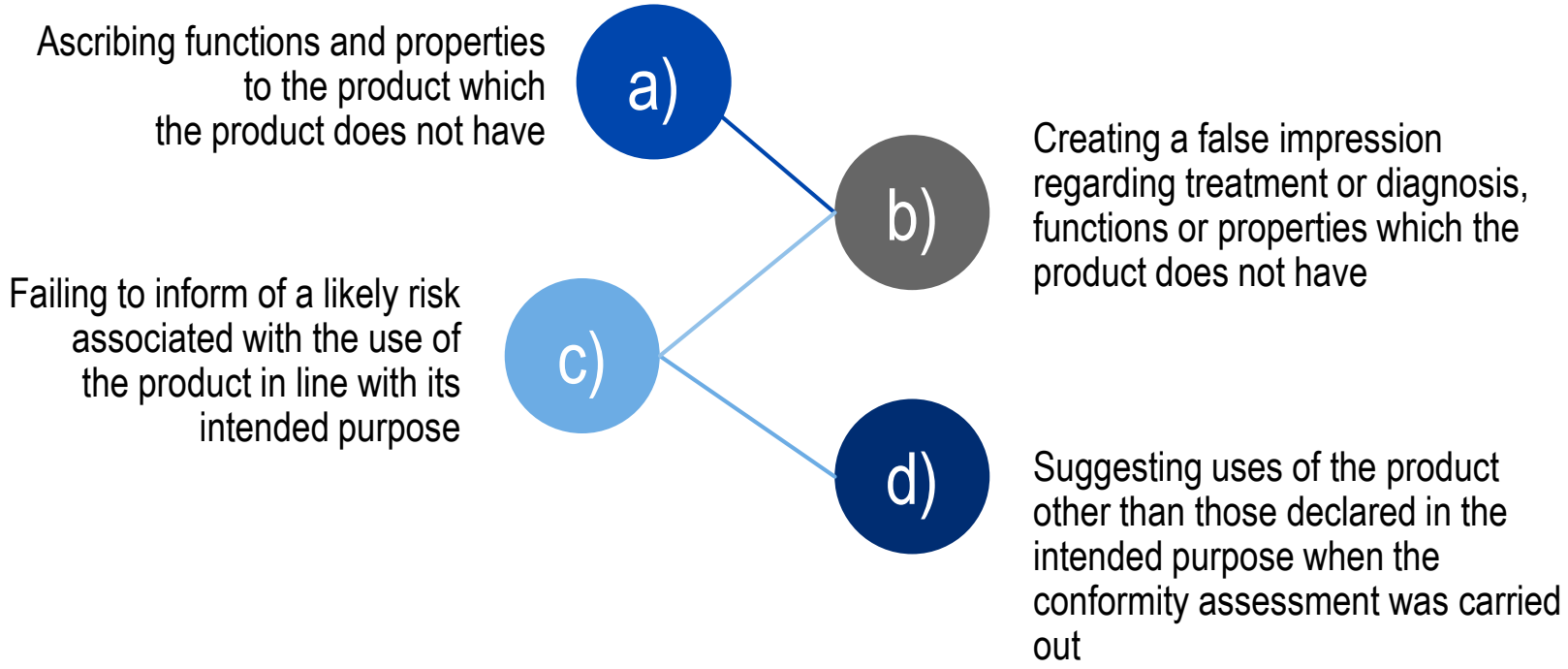
05 Installation and maintenance of an active Post Market Surveillance / Vigilance System

06 Technical Documentation including:

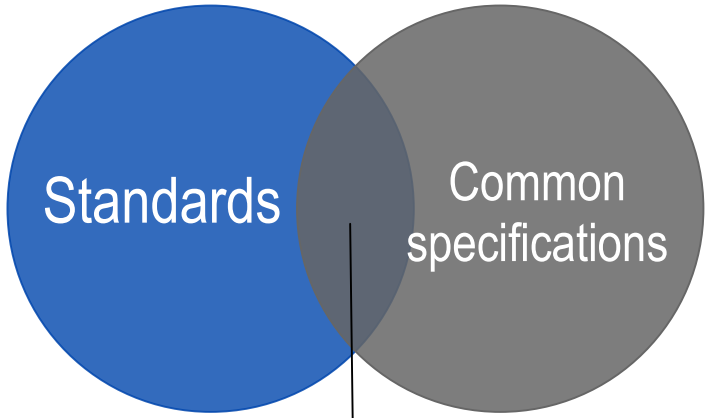
- Description and specifications of the device
- Information supplied by the Manufacturer
- Design, manufacturing and testing information
- General safety and performance requirements (e.g. standards applied)
- Risk Analysis and Risk Management
- Clinical Data supporting validation of the products

The MDR is requiring very specific and clear claims

In the labelling, instructions for use, making available, putting into service and advertising of devices, it is prohibited to use text, names, trademarks, pictures and figurative or other signs that may mislead the user or the patient with regard to the device's intended purpose, safety and performance by:

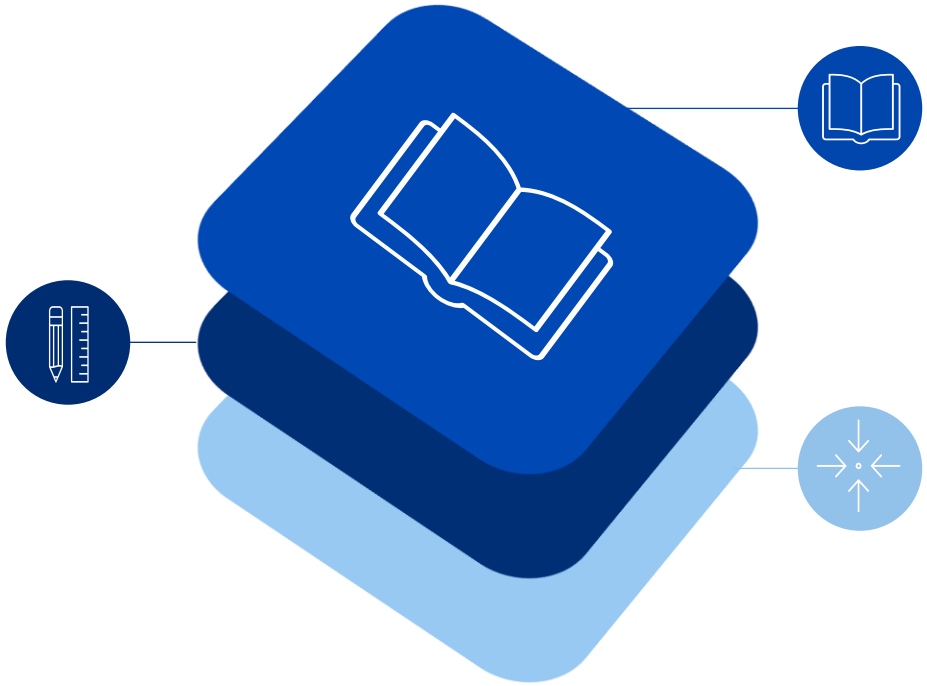


Article 9: Common Specifications



When existing standards seem insufficient, the Commission can create common specifications to compensate insufficient requirements

GSPR: General Safety and Performance Requirements



Chapter II
- Requirements reg. design & manufacture
- Clauses 10 - 22

Chapter III
- Requirements reg. device information
- Clause 23

Chapter I
- General requirements
- Clauses 1 - 9

Clause 23 of GSPR is requiring more transparency

Information supplied by manufacturer

- **Website to be updated**

IFU

- **Specification of clinical benefits to be expected**
- **Links to summary of safety & clinical performance**

Label

- Indication that device contains or incorporates
  1. a medicinal substance, incl. human blood or plasma derivative, or
  2. tissues/cells (or derivatives) of HO
  3. tissues/cells (or derivatives) of AO (commission regulation (EU) no. 722/2012)
- Unique Device Identification (UDI) carrier acc. Article 24 & Annex V Part C
- Qualitative composition of device & quantitative information on main constituents(s)

Design & Manufacturing Information

Identification of all sites, suppliers, sub-contractors

04

03

Data fully incl. into TD

Manufacturing processes

02

- Process validation
- Adjuvants
- Continuous monitoring
- Final product testing

01

Applied design stages

Structure of the MDR

New chapters

Chapter I (Art. 1-3):
Scope & definitions

Chapter II (Art. 5-24):
Making available on the market and putting into service of devices, obligations of economic operators, reprocessing, CE marking, free movement

Chapter III (Art. 25-34):
Identification and traceability of devices, registration of devices and of economic operators, summary of safety and clinical performance (SSCP), European database on medical devices

Chapter IV (Art. 35-50):
Notified bodies

Chapter V (Art. 51-60):
Classification and conformity assessment, consultations, scrutiny

Chapter VI (Art. 61-82):
Clinical evaluation & clinical investigation

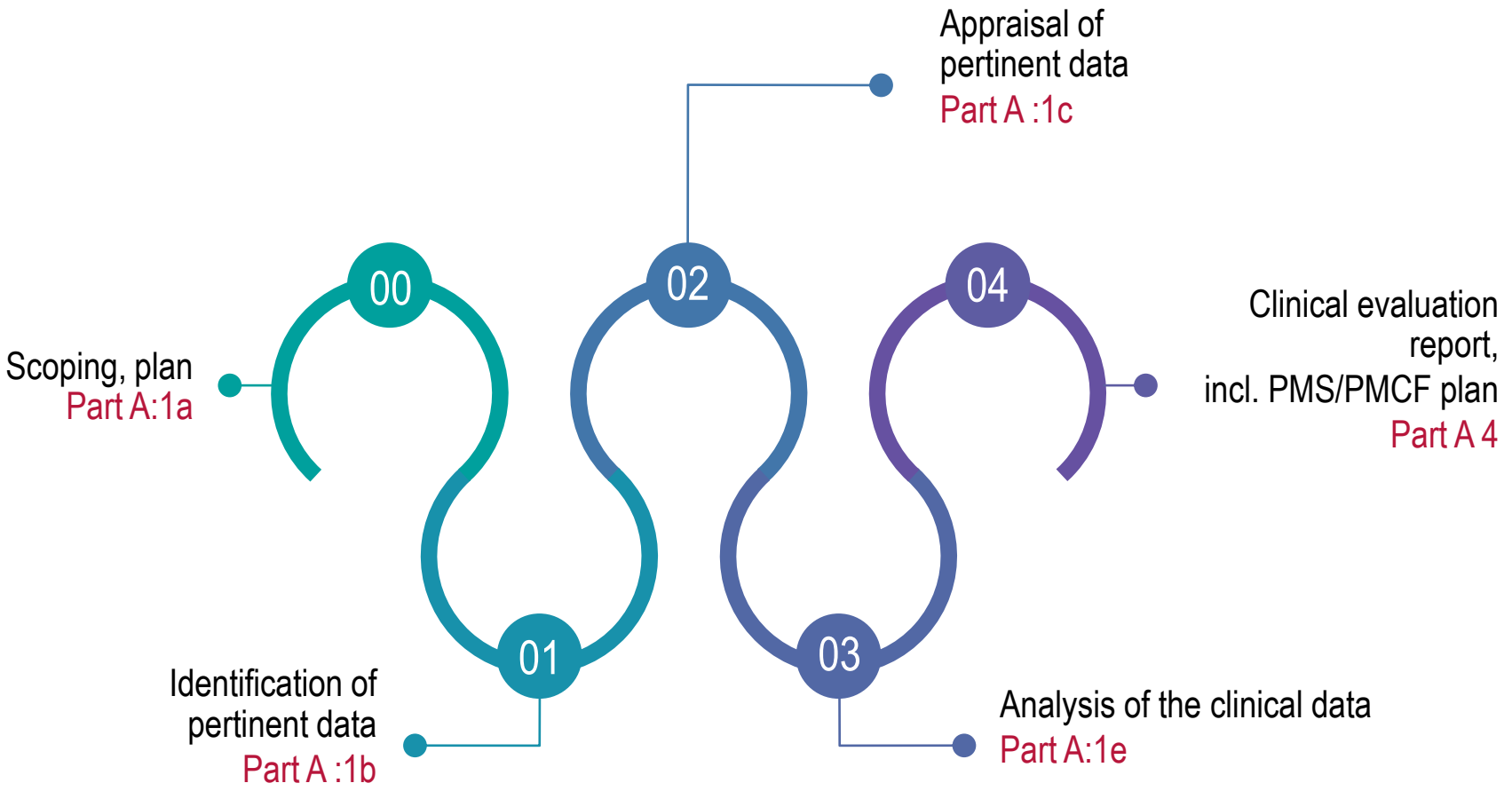
Chapter VII (Art. 83-100):
Post-market surveillance (PMS), post market clinical follow up (PMCF), vigilance, market surveillance, trends, periodic safety update report (PSUR)

Chapter VIII (Art. 101-108):
Cooperation between member states, expert laboratories, medical device coordination group, expert panels, device registers

Chapter IV (Art. 109-113):
Confidentiality, data protection, funding, penalties

Chapter X (Art. 114-123):
Final provisions

Art. 61 and Annex XIV, A: Will your compliance to MEDDEV help you?



Are you still allowed to and can you demonstrate equivalence?

- These characteristics shall be **similar to such an extent** that there would be **no clinically significant difference in the clinical performance and safety of the device**.
- Based on **proper scientific justification.**
- **Sufficient levels of access** to the data on devices to which Manufacturer is **claiming equivalence**
- **Results in CER , which is part of the TD**

In case no equivalence can be demonstrated clinical investigations need to be performed

Belongs your device to either the Class III or Implantable category?

Clinical investigations might not be relevant:

Clinical investigations expected for:

Equivalence same manufacturer

01 MDR - Art. 61, 4

Equivalence not same manufacturer

02 MDR - Art. 61, 5

Legacy devices

03 MDR - Art. 61,6a

List of devices, some of which were up classified

04 MDR - Art. 61,6b

Art. 52, 54 and Annexes IX.5, X.6: Mandatory Consultations

Clinical evaluation report (CER) of Manufacturer

Clinical evaluation assessment report (CEAR) of NB

Consultation

Type of device attributes	Time Initial /Change	Time NB estimate
Medicinal substances / device combinations	210 /60 days	X days
Human blood/plasma derivatives	210 /60 days	
Animal Origin (TSE)	4-12 weeks	
Human Origin	120/60 days	
Absorbables (purpose)	150 days	
Class III-Implantable	60 (21) days	
Class IIb active devices intended to administer and/or remove medicinal substances (rule 12)	60 (21) days	

Certification

Additional time needed

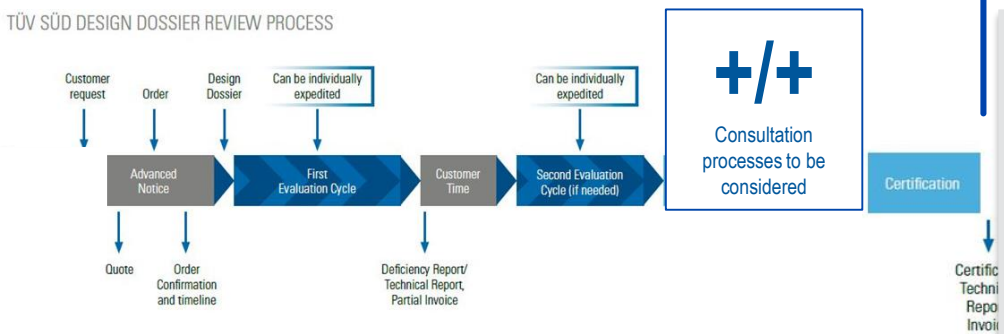
Article 54.3 and 55: Scrutiny

Class III implants and class IIb devices (rule 12) - after MDR - CE marking

Certification, NB Decisions,
Scrutiny / Notification

NB decides on Certification

NB issues the final Assessment Report, including a justification on divergent views (link to consultation process)



Art. 55: Scrutiny submission is required for cases were a consultation was performed.
By NB via EUDAMED /electronic system to
- **Competent Authorities**.

Include:
SSCP, IFU, Scientific Opinion, Assessment Report that includes justification on divergent views

Art 54.3: In any case when a **CER was assessed by NB a notification** via EUDAMED /electronic system to
- **Competent Authorities,**
- **National Authority responsible for NB and**
- **Commission** is required.

Include: **Clinical Evaluation Assessment Report** with a rational whether or not a consultation applied

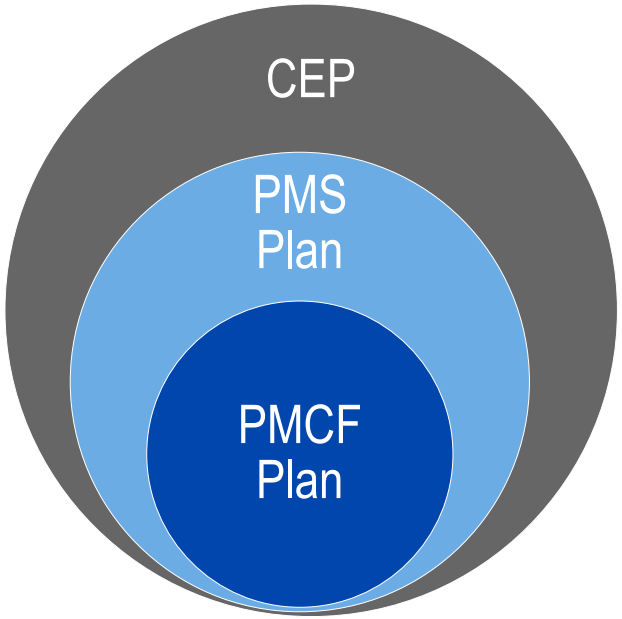
Annex III. 1.1b: The post-market surveillance plan

The post-market surveillance plan shall cover at least:

- A proactive and systematic process to collect any information
- The process shall allow a correct characterization of the performance of the devices and shall also allow a comparison to be made between the device and similar products on the market;
- Effective and appropriate methods and processes to assess the collected data;
- Suitable indicators and threshold values that shall be used in the continuous reassessment of the benefit- risk analysis and of the risk management
- Effective and appropriate methods and tools to investigate complaints and analyse market-related experience collected in the field;
- Methods and protocols to manage the events subject to the trend report as provided for in Article 88, including the methods and protocols to be used to establish any statistically significant increase in the frequency or severity of incidents as well as the observation period;
- Methods and protocols to communicate effectively with competent authorities, notified bodies, economic operators and users;
- Reference to procedures to fulfil the manufacturers obligations laid down in Articles 83, 84 and 86;
- Systematic procedures to identify and initiate appropriate measures including corrective actions;
- Effective tools to trace and identify devices for which corrective actions might be necessary; and
- A PMCF plan as referred to in Part B of Annex XIV, or a justification as to why a PMCF is not applicable.

Art. 83, 84: PMS and Annex II + III, XIV, B: PMCF

- **PMCF** is a continuous process to update the clinical evaluation and is part of the PMS plan
- The **manufacturer** shall proactively collect & evaluate clinical data…with the aim of:



- Confirm the safety & performance throughout expected lifetime
- Identify previously unknown side-effects
- Monitor the identified side-effects and contraindications
- Identify and analyze emerging risks on the basis of factual evidence
- Ensure the continued acceptability of benefit /risk ration
- **Identify systematic misuse or off-label use, with a view to verify that the intended purpose is correct**
- Consider any preventive & corrective actions

Annex XIV Part B: PMCF - Plan

- **PMCF** plan shall include:

- **General methods & procedures** of PMCF to be applied, such as gathering of clinical experience gained, feedback from users, screening of scientific literature and of other sources of clinical data;
- **Specific methods & procedures** of PMCF to be applied, such as evaluation of suitable registries or PMCF studies;
- Rationale for the appropriateness for above points
- Reference to the relevant parts of the clinical evaluation report and to the risk management
- Specific objectives to be addressed by the PMCF
- Evaluation of the clinical data related to equivalent or similar devices
- Reference to relevant CS, standards and guidance on PMCF
- Detailed & adequately justified time schedule for PMCF activities (e.g. analysis of PMCF data and reporting) to be undertaken by the manufacturer

Article 61.11 & 61.12: Clinical Evaluation

61. 11. The clinical evaluation ***(process)*** and its documentation ***(plans and reports)*** shall be **updated throughout the life cycle** of the device concerned with clinical data obtained from the implementation of the **manufacturer's PMCF plan** in accordance with Part B of Annex XIV and the **post-market surveillance (PMS) plan** referred to in Article 84.

For **class III devices and implantable devices,** the **PMCF evaluation report** and, if indicated, the **summary of safety and clinical performance (SSCP)** referred to in Article 32 shall be updated **at least annually with such data.**

61.12.**The clinical evaluation, its results and the clinical evidence** derived from it shall be documented in a **clinical evaluation report** as referred to in Section 4 of Annex XIV, which, except for custom-made devices, shall be **part of the technical documentation** referred to in Annex II relating to the device concerned.

Article 86: Periodic Safety Update Report (PSUR)

- Conclusion on benefit risk determination
- Main findings of PMCF Report

- Sales volume of devices & estimate of population using device involved
- Where practicable, usage frequency of device.

Article 86: Periodic Safety Report Update (PSUR)

CE-marked Devices

- The PSUR shall be updated at least **annually** for **Class IIb and Class III devices.**

- **Updated every two years** for **Class II a**

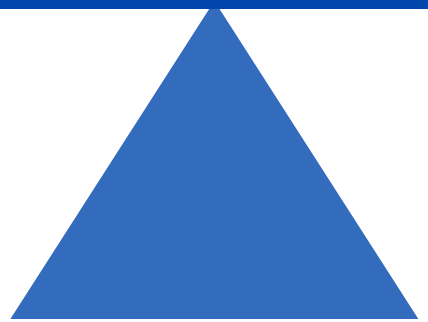
Custom-made Devices

- PSUR shall be part of the technical documentation as specified in Annexes II and III.

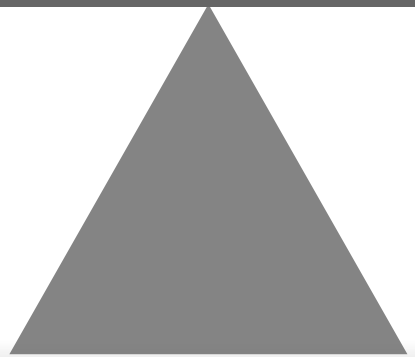
- PSUR shall be part of the documentation referred to in Section 2 of Annex XIII.

Article 32: Summary of safety & clinical performance (SSCP)

In case of **class III & implantable devices**, other than custom-made or investigational devices, manufacturer shall draw up a SSCP



Manufacturer shall mention on **label or IFU** where the SSCP is available



The SSCP shall be…

written in a way that is clear to the intended **user and, if relevant, to the patient**

made available to public via Eudamed

part of the conformity assessment in accordance with Article 52

validated by NB

NB has to upload validated final SSCP to Eudamed

SSCP shall include at least the following aspects:

- **Identification of the device and the manufacturer**, incl. basic UDI-DI and single registration number SRN
- **Intended purpose** of device, incl. indications, contra-indications & target populations
- **Device description**, incl. a reference to previous generation(s) or variants if such exist, and the description of the differences, as well as a description of the accessories, other medical devices and other products that are not medical devices, which are intended to be used in combination with the medical device
- **Possible diagnostic or therapeutic alternatives**
- **Reference to harmonized standards and common specifications**
- **Summary of clinical evaluation** as referred to in annex XIII, and relevant information on **PMCF**
- **Suggested profile and training for users**
- **Information** on any **residual risks** and any **undesirable effects, warnings and precautions**

Thank you!